UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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IN RE ELAN CORP. SECURITIES LITIGATION

05 Civ. 2860 (RJH)

**MEMORANDUM ORDER AND OPINION**

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This is a class action lawsuit for securities fraud under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (the "1934 Act") and Securities and Exchange Commission ("SEC") Rule 10b-5 promulgated thereunder. 15 U.S.C. §§ 78j(b), 78t(a); 17 C.F.R. § 240.10b-5. Lead Plaintiffs ("Plaintiffs") are one individual and five institutional investors that purchased securities of defendant Elan Corporation PLC ("Elan") between February 18, 2004 and February 28, 2005 (the "Class Period"). (¶¶ 33–39.)[1] Defendant Elan is a public biotechnology company incorporated under the laws of Ireland whose activities include the development of biopharmaceutical products to treat neurologic disorders, autoimmune disorders, and chronic pain. (¶ 40.) During the Class Period, defendant G. Kelly Martin ("Martin") was Elan's Chief Executive Officer, defendant Shane M. Cooke ("Cooke") was Elan's Chief Financial Officer, and defendant Lars Ekman ("Ekman") was Elan's Executive Vice President and President of Research and Development. (¶¶ 43–44.) Martin and Cooke were also directors for Elan during the Class Period. (¶¶ 43–44.)[2]

Plaintiffs claim they purchased Elan securities at prices that were inflated as a result of Defendants' material misrepresentations and omissions regarding the "purported

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[1] "¶" and "¶¶" indicate citations to the numbered paragraph(s) of Plaintiffs' Consolidated Class Action Complaint ("Complaint").

[2] Martin, Cooke, and Ekman are collectively referred to as the "Individual Defendants."

safety, commercial viability, and projected market share" of the drug Tysabri. (¶¶ 4, 33–39.) Tysabri was developed and tested by Elan in collaboration with Biogen IDEC, Inc. ("Biogen") as a potential treatment for conditions including multiple sclerosis ("MS").[3]

## BACKGROUND

### I. Allegations in Plaintiffs' Complaint

The following summary is drawn from the allegations of Plaintiffs' Consolidated Class Action Complaint ("Complaint") and from documents incorporated or relied upon by Plaintiffs in drafting the Complaint. *See, e.g., Brass v. Am. Film Techs., Inc.*, 987 F.2d 142, 150 (2d Cir. 1993).

#### A. Collaboration agreement

On August 17, 2000, Elan and Biogen announced their Antegren[4] Development and Marketing Collaboration Agreement (the "Collaboration Agreement") to develop and commercialize Tysabri, a potential treatment for MS, Crohn's disease, and rheumatoid arthritis ("RA"). (¶¶ 80–81.) The drug was described in a press release as having "blockbuster potential." (¶ 80.)

The Collaboration Agreement established a Joint Steering Committee, which was comprised primarily of "senior management" of Elan and Biogen. (¶¶ 78, 82–84.)

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[3] Recently, the District of Massachusetts dismissed a class action lawsuit against Biogen based on similar allegations to those made in Plaintiffs' Complaint. *See In re Biogen Idec Sec. Litig.*, No. 05-10400-WGY (D. Mass. Oct. 25, 2007). The court granted Biogen's motion to dismiss for failure to adequately plead scienter. *See id.* at 24.

[4] Antegren was the original name for Tysabri. Tysabri is the trade name for a monoclonal antibody also known as natalizumab and anti-VLA-4 antibody. (*See, e.g.*, Mem. Supp. Elan Defs.' Mot. Dismiss Consol. Class Action Compl. ("Defs.' Br.") 3; April 20, 2007 Declaration of Jaculin Aaron ("Aaron Decl.") Ex. 15 at 372.)

Through the Joint Steering Committee, the two companies shared positive and negative information regarding Tysabri. (¶ 82.)

The Collaboration Agreement also established a Joint Project Team and a Joint Commercialization Team, each of which included Elan and Biogen representatives and reported to the Joint Steering Committee. (¶¶ 82, 86, 87). The Joint Project Team was responsible for aspects of research, development, and clinical testing of Tysabri. (¶¶ 82, 86.) The Joint Commercialization Team was responsible for commercialization activities and worked in coordination with the Joint Project Team "in developing and implementing standard operating procedures for adverse event reporting." (¶ 87.)

The Collaboration Agreement required Defendant Martin to meet with Biogen Chief Executive Officer James Mullen twice each year to discuss Tysabri development, commercialization, and other issues. (¶ 88.) Mullen stated in July and November 2004 that he was "in frequent communication" with defendant Martin. (¶¶ 88, 151.)

Under the Collaboration Agreement, both Elan and Biogen had access to clinical and preclinical data, including data regarding adverse drug events. (¶ 90.) The Collaboration Agreement also required Elan and Biogen to "fulfill all of their safety surveillance and pharmacovigilance regulatory obligations" related to Tysabri and to set up procedures for the reporting of adverse event data to the responsible party, and to disclose and make available all preclinical and clinical information. (¶¶ 89–91.)

**B. Tysabri clinical trials**

Elan and Biogen conducted clinical trials to evaluate the safety and efficacy of Tysabri as part of their efforts to receive FDA approval to market and sell Tysabri to the

public. (¶¶ 92–94.) Elan was primarily responsible for Crohn's disease and RA trials, and Biogen was primarily responsible for MS trials.[5] (¶ 94.)

In order to receive approval from the FDA to market a drug to the public, a sponsor must conduct three phases of clinical trials designed to assess the safety and efficacy of the drug product. (¶ 93); *see also* 21 C.F.R. § 312.21. During Phase I, the drug is administered to a small number of healthy participants in order to determine the proper dosage of the drug, to characterize its metabolism and excretion, and to identify acute side effects. (¶ 93.) Phase II trials include patients who suffer from the medical condition the drug is designed to treat; these trials are used to gather safety data and preliminary efficacy data. (¶ 93.) If the results of Phase II trials suggest that the drug is safe and effective, Phase III trials investigate the effects of the drug in a much larger patient population. (¶ 93.)

According to FDA regulations, a pharmaceutical company "sponsor" is the entity that takes responsibility for and initiates a clinical trial. 21 C.F.R. § 312.3. The sponsor then hires "investigators" to conduct the clinical investigation—it is under the investigators' immediate direction that drugs are administered or dispensed to subjects. *Id.* A pharmaceutical company sponsor may use its own employees as investigators. *Id.* It is unclear from the Complaint whether the investigators in the Tysabri clinical trials were employees of Elan or Biogen.

FDA regulations require a sponsor to keep written documentation of all adverse events that occur during clinical trials, *id.* § 310.305(a), to report adverse events that are both "serious" and "unexpected" within 15 days, and to report any "unexpected fatal or

[5] MS is an autoimmune disorder in which the body's immune system attacks myelin, a fatty tissue which surrounds and protects nerve cells and is essential to their proper functioning. (¶¶ 62–65.)

life-threatening experience" to the FDA as soon as possible, *id.*. § 312.32(c). In addition, the sponsor must promptly inform the FDA and all investigators of all "significant new adverse effects or risks" concerning the drug. *Id.* § 312.50.

Phase I clinical trials of Tysabri were conducted by Athena Neurosciences in December 1995.[6] (¶ 98.) In September 2001, Elan and Biogen announced "promising data" from Phase II clinical trials showing Tysabri's efficacy as a treatment for MS. (¶ 99.)

Phase III clinical trials investigating Tysabri's efficacy against MS consisted of two large two-year trials. (¶ 100.) These trials were designed as double-blind, placebo-controlled studies. (April 20, 2007 Declaration of Jaculin Aaron ("Aaron Decl.") Ex. 4 at 27–28.[7]) The drug was administered to ensure that neither the sponsor, subjects, physicians, nurses, nor other study personnel knew whether a subject was receiving Tysabri, except, for example, in the event of a medical emergency. (*Id.* Ex. 4 at 28–29.) In the Tysabri Phase III MS trials, a "Treating Neurologist" oversaw the assessment of adverse events. (*Id.* Ex. 4 at 29.) According to the information provided to the FDA, all adverse events (defined as "any untoward medical occurrence experienced by a subject") that occurred during the Tysabri clinical trials were recorded. (*Id.* Ex. 4 at 60–61.)

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[6] Athena Neurosciences was acquired by Elan in 1996. (¶ 98.)

[7] Exhibit 4 to the Aaron Declaration is the Medical Review prepared by The Center for Drug Evaluation and Research ("CDER"), the FDA division that reviewed the data submitted hy Defendants in their May 2004 Biologics License Application ("BLA") for Tysabri. (Aaron Decl. Ex. 4 at 55.) The November 23, 2004 memorandum of Dr. David Ross, a CDER Deputy Director, summarizes the safety and efficacy data and analysis in the CDER Medical Review. (*See, e.g., id.* Ex. 17 at 4, 8, 9, 12.) In their Complaint, Plaintiffs rely upon and cite to the sections of Dr. Ross's memorandum regarding Tysabri's safety. (*See* ¶¶ 16, 140.) Plaintiffs therefore had knowledge of the CDER Medical Review and relied upon it in drafting their Complaint. Accordingly, it is appropriate for the Court to consider this document in connection with Defendants' Rule 12(b)(6) motion to dismiss. *See, e.g., Brass,* 987 F.2d at 150.

The "AFFIRM" trial (Study 1801) involved over 900 patients at 99 sites worldwide and tested the efficacy of Tysabri as a monotherapy for MS. (¶¶ 100, 310; Aaron Decl. Ex. 4 at 35–36.) The first subject in the AFFIRM trial began treatment on November 6, 2001. (Aaron Decl. Ex. 4 at 36.) The "SENTINEL" trial (Study 1802) involved approximately 1,200 patients and tested the efficacy of Tysabri in combination with Avonex, an existing MS drug made by Biogen. (¶ 100; Aaron Decl. Ex. 4 at 36.) The first subject in the SENTINEL trial began treatment on January 14, 2002. (Aaron Decl. Ex. 4 at 36.)

Elan and Biogen also conducted clinical trials to investigate Tysabri's potential as a treatment for Crohn's disease and RA. (¶¶ 102–04.) With respect to Crohn's disease, Phase II trials were completed by May 23, 2001, and two Phase III trials, "ENACT-1" and "ENACT-2," began in December 2001. (¶ 102.) ENACT-1 was completed by July 24, 2003 and ENACT-2 was completed by January 29, 2004. (¶¶ 102–03.) On January 29, 2004, Elan began a third Phase III Crohn's disease trial, called "ENCORE." (¶ 103.) In mid-2004, Elan initiated Phase II RA trials. (¶ 104.)

On February 18, 2004, Defendants announced that they intended to seek "fast-track" FDA approval of Tysabri as a treatment for MS based on the results of "one year data" from Phase III MS trials.[8] (¶ 101; Aaron Decl. Ex. 2.) In May 2004, Defendants submitted a Biologics License Application ("BLA") to the FDA, requesting fast-track approval. (¶ 95.) The FDA designated Tysabri for "priority review" and "accelerated

[8] In fact, Defendants did not submit precisely one year of treatment data for each subject. (*See* Aaron Decl. Ex. 4 at 25–26, Ex. 17 at 5.) The clinical trial protocol provided that data analysis would occur after subjects had undergone an average of one year of treatment. (*See id.* Ex. 4 at 25, Ex. 17 at 5.) The data submitted to the FDA reflected an average of thirteen months of treatment data per patient, but different durations for different subjects, who began treatment at different times. (*See id.* Ex. 4 at 25–26, Ex. 17 at 5.) (*See id.* Ex. 17 at 5.) Defendants, as well as the FDA, refer to these data as "one-year data" as a "convenient approximation." (*See id.* Ex. 4 at 26.)

approval" and granted the BLA on November 23, 2004. (¶ 95.) Under the terms of the "accelerated approval" program, however, Elan and Biogen were still required to complete their Phase III MS trials. (¶¶ 95, 97.)

### C. Withdrawal of Tysabri

On February 7, 2005, Dr. Daniel Pelletier, a physician at the University of California, San Francisco admitted to the hospital a Tysabri MS trial subject who presented with unilateral weakness, slurred speech, and cognitive impairment. (¶ 300.) Though other neurologists said these symptoms might be caused by the patient's MS, Pelletier believed these symptoms were not typical of MS. (¶ 300.) Instead, Pelletier believed the symptoms were typical of a disease known as progressive multifocal leukoencephalopathy ("PML"). (¶¶ 67, 300.) Pelletier "immediately" informed Biogen of his opinion. (¶ 300.)

PML is a rare, usually fatal condition caused by an infection of the brain by a polyoma virus known as the JC virus. (¶¶ 67, 68, 318; Aaron Decl. Ex. 12.[9]) The JC virus is present and latent in almost all healthy adults but can infect the brain and multiply rapidly in individuals with compromised immune systems. (¶¶ 67, 68.) Therefore, PML is typically seen in patients with severely impaired immune systems, such as AIDS patients. (¶¶ 67, 68, 322.) However, because activation of the JC virus causes removal of myelin cells, the same cells that are damaged in MS patients, PML is

[9] Exhibit 12 to the Aaron Declaration is a New York Times article that Plaintiffs rely upon in their Complaint. (*See* ¶¶ 12, 329.)

somewhat similar to, and may be confused with, MS. (Aaron Decl. Ex. 5 at 150,[10] Ex. 12 at 2.)

On February 28, 2005, Elan and Biogen announced in a joint press release that they were halting all ongoing Tysabri clinical trials and suspending Tysabri sales indefinitely due to one confirmed, fatal case and one suspected, nonfatal case of PML in patients participating in MS clinical trials. (¶¶ 105, 318.) No other reason was given for the decision to withdraw the drug and Plaintiffs do not allege that there were other, undisclosed reasons for this announcement. According to Defendants, both of these patients had received Tysabri in combination with Avonex, another MS drug, for more than two years. (¶ 318.) That same day, Elan American Depository Share ("ADS") and common stock share prices fell by 70% and 68%, respectively, in response to the announcement. (¶ 324.)

On March 4, 2005, Bloomberg L.P. reported that the suspected case of PML reported on February 28 had been confirmed. (¶ 334.) That day, Elan ADS and common stock share prices fell by 14% and 13%, respectively. (¶ 334.)

On March 31, 2005, the Boston Globe reported a third case of PML in an individual who had received eight doses of Tysabri over eighteen months while participating in a Tysabri Crohn's disease trial. (¶ 338.) This patient had been misdiagnosed in June 2003 with malignant astrocytoma, a type of brain cancer, and had died in December 2003. (¶ 338.) This patient had not been taking Tysabri in combination with Avonex, but had in the past taken other immunosuppressive drugs. (¶ 338.) In response to the news, Elan ADS and common stock shares fell by 56%.

[10] Exhibit 5 to the Aaron Declaration is a transcript of testimony given on March 7, 2006 at the March 2006 FDA Hearing, which is quoted from and cited by Plaintiffs in the Complaint. (*See, e.g.*, ¶¶ 130, 141–46, 148–50.)

In total, in the time between the initial announcement regarding the withdrawal of Tysabri on February 28, 2005 and the report of the third PML case on March 31, 2005, Elan securities lost 90% of their value. (¶ 342.)

According to Elan's April 11, 2005 Form 10-K disclosure, the SEC initiated an "informal inquiry" into Elan's actions and securities trading relating to the February 28, 2005 withdrawal of Tysabri from the market. (¶ 343.) The SEC also filed a settlement enforcement action against Thomas Bucknam, a Biogen executive, for selling almost 90,000 shares of Biogen stock on February 18, 2005 after learning that day that a patient taking Tysabri had been diagnosed with PML. (¶ 344.) Bucknam eventually paid three million dollars to the SEC in settlement. (¶ 344.)

**D. Tysabri's reintroduction to the market**

On September 26, 2005, Elan and Biogen announced that they had submitted a supplemental BLA to the FDA proposing that Tysabri be reintroduced to the market with more limited distribution and a new warning label. (¶ 348.) On February 16, 2006, Elan and Biogen announced that the FDA had lifted the hold on Tysabri clinical trials and that they would be initiating a Tysabri monotherapy trial in the coming weeks. (¶ 351.)

On March 7 and 8, 2006, an FDA advisory committee held a hearing regarding Elan and Biogen's proposal regarding Tysabri (the "March 2006 FDA Hearing") and voted on whether Tysabri should be allowed to return to the market. (¶ 354.) The committee voted 12-0 to recommend Tysabri for treatment in relapsing forms of MS. (¶ 354.)

On June 5, 2006, the FDA announced that it had approved Tysabri's return to the market, subject to a "special restricted distribution program" under which Tysabri was

not to be used in combination with other drugs and was only to be used in "patients who have not responded adequately to, or cannot tolerate" other MS treatments. (¶ 357.) In addition, Tysabri was required to bear a prominent "black-box" warning label, the strongest required by the FDA, which warned of the risk of PML and discouraged use with other immunomodulatory therapies or in immunocompromised patients. (¶¶ 358–59; Aaron Decl. Ex. 10.[11]) Tysabri would also be subject to a risk management program that required registration of prescribers and infusion centers, distribution only to enrolled patients who met all conditions of the program, preliminary MRI scans of recipients prior to treatment, and regular evaluation of patients. (¶¶ 358–60.)

In July 2006, Tysabri was reintroduced to the market with the restrictions and limitiations described above. (¶ 363.)

**E. "Red flags" allegedly ignored by Defendants**

Plaintiffs allege that Defendants knew of or recklessly disregarded various "red flags" indicating that Tysabri had limited commercial potential due to significant safety issues. (¶ 108.) These "red flags" fall into three categories: (1) that Tysabri was "by its very nature" an immunosuppressive drug that left patients vulnerable to serious opportunistic infections; (2) that animal studies by Defendants and others, scientific articles, and remarks of "top scientists" at scientific meetings indicated the serious risks associated with Tysabri due to its severe immunosuppressive effects; and (3) that numerous "serious opportunistic infections" had occurred during the Tysabri clinical trials before the class period. (¶ 108.)

[11] Exhibit 10 to the Aaron Declaration is a copy of the revised drug labeling for Tysabri following its return to the market in 2006. Plaintiffs quote from and rely upon the revised Tysabri labeling in the Complaint. (*See, e.g.*, ¶¶ 360–62.)

### 1. Tysabri's "inherent" immunosuppressive effects

Plaintiffs allege that Tysabri, because it "prevents white blood cells from migrating to an infected area of the body" is an inherently immunosuppressive and dangerous drug. (¶ 109.) As a result, Plaintiffs allege that there was a "substantial risk" that Tysabri would cause "serious, frequently life-threatening opportunistic infections." (¶¶ 109–10.)

Tysabri is believed to act by binding to a protein called alpha-4 integrin, which is found on the surface of certain cells of the immune system. (Aaron Decl. Ex. 4 at 8, 12, Ex. 10 at 2.) Alpha-4 integrin normally functions to allow these immune cells to enter the central nervous system ("CNS") from the bloodstream by crossing the so-called "blood-brain barrier." (*See, e.g., id.* Ex. 10 at 2, Ex. 13, Ex. 14, Ex. 15, Ex. 16.)[12] In MS, the body's own immune system improperly attacks and damages CNS tissue. (*See, e.g., id.* Ex. 4 at 11–12, Ex. 13.) By binding to alpha-4 integrin, Tysabri is thought to interfere with the interactions necessary for the immune cells to cross the blood-brain barrier and cause damage in MS patients. (*See, e.g., id.* Ex. 4 at 12.) According to Plaintiffs, "[o]pportunistic infections occur when ordinarily benign organisms infect individuals with severely impaired immune systems. These ordinarily benign organisms . . . very rarely produce disease in healthy humans with intact immune systems." (¶ 3 n.4.) Plaintiffs' argument seems to be that, since Tysabri was believed to function by suppressing one component of the immune response, Defendants knew or should have known that it would cause severe immunosuppression in a human patient, leaving the patient vulnerable to infections such as PML.

[12] Exhibits 13, 14, 15, and 16 to the Aaron Declaration are scientific journal articles cited and relied upon by Plaintiffs in the Complaint. (*See, e.g.*, ¶¶ 71, 121, 123, 125.)

### 2. Animal study data and warnings from scientists

Plaintiffs contend that information including data from animal studies, published scientific articles, and talks at scientific meetings revealed the "serious, life-threatening risks" posed by Tysabri. (¶¶ 98–129, 175.)

With respect to animal study data, Plaintiffs assert that Tysabri's "serious, life-threatening risks" were apparent from "unexplained" deaths of Tysabri-treated animals in studies conducted by Elan, Biogen, and Athena Neurosciences. (¶ 112.) The results of these studies were "made available to senior executives" of Elan and Biogen. (¶¶ 111–12.) According to Plaintiffs' own allegations, however, almost all of these deaths were not in fact "unexplained," but instead were attributed by the investigators to causes other than Tysabri administration. (¶ 112.)

Plaintiffs also allege that Tysabri's risks had been recognized by various scientists, including Dr. Lawrence Steinman, a researcher who was involved in the early development of Tysabri. (¶¶ 70, 120–29; Aaron Decl. Ex. 12.) Dr. Steinman was involved in an early animal study that led to the development of Tysabri in the early 1990s.[13] (¶ 70.) Dr. Steinman told Plaintiffs' attorneys in July 2005 that he had concluded based on this study that Tysabri could potentially leave a patient vulnerable to opportunistic infections because it prevented migration of white blood cells to other organs besides the brain. (¶¶ 70, 72–74, 113.) Dr. Steinman also wrote in a July 2004 article that there was "at least a theoretical concern that recipients of [Tysabri] would become generally compromised in their ability to fight infection," and noted that increased rates of an upper respiratory tract infection had been observed in Phase II MS

[13] Dr. Steinman is also the co-founder and director of Bayhill Therapeutics, a competitor of Elan and Biogen in the market for MS drugs. (Aaron Decl. Ex. 12.)

trials.[14] (¶ 121.) At some time after publication of the July 2004 article, Biogen executives asked Dr. Steinman to "tone down" his criticisms of Tysabri. (¶ 122.)

Dr. Steinman again warned of the risks of opportunistic infections from Tysabri at scientific conferences in September 2004 and January 2005. (¶ 128.) Elan and Biogen scientists and physicians frequently attended conferences such as these, and Biogen co-sponsored the January 2005 conference. (¶ 128.)

Sometime in 2004, Dr. Elliott Obi-Tabot wrote a research paper as a consultant for a competitor of Elan and Biogen in which he expressed "concerns about the potent immunosuppressive properties of Tysabri and concluded that serious opportunistic infections were a possible side effect." (¶ 124.)

A May 2003 article by researchers at Merck Research Laboratories also mentioned the fact that VLA-4 antagonists like Tysabri may have "unacceptable side effects, such as greater risk of infection caused by impairment of phagocytic leukocyte migration and function." (¶ 125; Aaron Decl. Ex. 15.)[15]

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[14] Elsewhere in the article, Steinman stated that Tysabri "has shown some degree of success in phase 2 clinical trials of MS and in inflammatory bowel disease." (Aaron Decl. Ex. 13 at 214.) The article, read in its entirety, is not strongly critical of Tysabri. Other of Plaintiffs' alleged "red flags" are simply not on point. For example, Plaintiffs allege that Dr. Stephen Miller, employed by Biogen to work on Tysabri development from 1999 to 2001, co-authored an article reporting animal studies of Tysabri in which he states that Tysabri "may be problematic in treating established autoimmune disorders such as MS." (¶¶ 115–16.) Dr. Miller claims that he reported his concerns to senior Biogen officials and recommended additional testing in animals, but Biogen did not conduct these studies and ultimately terminated Dr. Miller's research. (¶¶ 117–18.) Dr. Miller's concerns, as described in Plaintiffs' Complaint, are not related to Tysabri's immunosuppressive effects but instead relate to its efficacy against MS, specifically the possibility that it may exacerbate MS or promote relapse. (¶¶ 115–18.) Plaintiffs also describe an August 1999 article describing a study funded by Elan that included the statement, "[f]urther studies will be required to determine the longer effect of [Tysabri] treatment." (¶ 123.) However, it is clear in context that this statement simply referred to the fact that the study only addressed short-term Tysabri treatment. (Aaron Decl. Ex. 16.) The article does not address the immunosuppressive effects of Tysabri. (*Id.*)

[15] Plaintiffs also cite an article by Dr. Olaf Stuve published in May 2006 but offer no explanation how the Defendants could have known or disclosed the information in this article prior to its publication. (¶¶ 126–27.)

### 3. The occurrence of PML and other "serious opportunistic infections"

#### a) PML

Plaintiffs do not allege that Defendants were actually aware of any diagnosis of PML associated with Tysabri at any time before February 2005. However, Plaintiffs point out that Biogen and Elan have acknowledged that the two patients in the SENTINEL trial who had developed PML had shown neurological problems as early as October 2004. (¶¶ 312, 317.)

A February 28, 2005 memorandum sent by Biogen and Elan to physicians stated that one patient was hospitalized on February 12, 2005 and underwent an MRI that "suggested a differential diagnosis that included PML." (¶ 313.) According to Plaintiffs, the MRI showed lesions that were typical of PML but not typical of MS. (¶ 313.) This patient's autopsy report revealed that he had experienced symptoms of PML in October 2004 and that the symptoms had worsened by December 2004. (¶ 313.) Furthermore, Plaintiffs' Confidential Source No. 9 ("CS 9"), a senior scientist at NIH who had researched PML and the JC virus for twenty-five years, said that the brain of this patient contained more JC virus than this researcher had ever seen in a patient. (¶¶ 166, 314.)

The memo also stated that a second patient had developed symptoms consistent with PML in December 2004. (¶ 315.) A June 2005 article in the New England Journal of Medicine contained additional information about this patient. (¶ 315.) In October 2004, this patient was found to have atypical frontal lesions, which Plaintiffs allege are a symptom of PML. (¶ 315.) In December 2004, additional lesions consistent with a diagnosis of PML were found, and the attending physicians discontinued the patient's Tysabri treatment. (¶ 315.)

Dr. Burt Adelman, the executive vice president of development for Biogen, stated in March 2005 that the symptoms of PML in these two patients "started much earlier than when the diagnosis was made." (¶ 316.) Dr. Adelman also stated that one patient had been diagnosed with PML more quickly but "the prudent action was not taken." (¶ 316.)

Dr. Michael Panzara, a Biogen clinical neurologist, reported at the March 2006 FDA Hearing that a second Tysabri-related death from PML had occurred in December 2003 during a Tysabri Crohn's disease trial, but that this patient had originally been misdiagnosed in July 2003 with malignant astrocytoma, a type of brain cancer. (¶ 149; Aaron Decl. Ex. 5 at 61.) Plaintiffs' Confidential Source No. 8 ("CS 8"), a Professor of Neurology with expertise in MS and immunology, concluded that the July 2003 diagnosis of malignant astrocytoma in this patient was "highly suspicious" and suggested that this diagnosis was either the result of malpractice or of a deliberate attempt to conceal the diagnosis of PML. (¶¶ 166, 167.) CS 8 opined that no competent neuropathologist could have misdiagnosed this patient (¶¶ 166, 167), pointing out that the neuropathologist who reevaluated this death in March 2005 determined in only ten minutes that the cause of death was PML, not malignant astrocytoma (¶ 167). CS 9 agreed, stating that malignant astrocytoma and PML are "completely dissimilar" and that "any neuropathologist with any skill" would not have diagnosed PML in this patient. (¶ 166.)

**b) Non-PML opportunistic infections**

Plaintiffs allege that Defendants were aware that Tysabri caused other "serious opportunistic infections" in addition to PML. (*See, e.g.*, ¶¶ 153–161.) Plaintiffs allege that testimony at a March 2006 FDA Hearing revealed that various "serious opportunistic infections and deaths occurred" during Tysabri clinical trials "well before" Defendants

applied for fast-track approval (¶ 130) and that Defendants knew of these events (¶ 5). Dr. Alice Hughes of the FDA stated that thirteen of seventeen deaths that occurred during the Tysabri clinical trials were in patients receiving Tysabri, and that two of these deaths were caused by non-PML opportunistic infections. (¶ 143; Aaron Decl. Ex. 5 at 185.)

Dr. Panzara presented safety data at the hearing on behalf of Biogen and Elan and concluded that the clinical trial data indicated that Tysabri treatment is associated with an increased risk of PML and that "there may also be an increased risk of other opportunistic infections." (¶ 150.) Specifically, Dr. Panzara disclosed that at least eleven types of opportunistic infection had occurred during the clinical trials. (¶ 144.) He also stated that herpes infections, which had been examined as a "marker of potential effects of [Tysabri] on cell-mediated immunity," had occurred with greater frequency in patients receiving Tysabri. (¶ 145; Aaron Decl. Ex. 5 at 58.) Dr. Hughes commented that the infections observed during the clinical trials suggested "the possibility of a compromise in cell-mediated immunity." (¶ 144; Aaron Decl. Ex. 5 at 180.)

Plaintiffs also reviewed adverse event reports received by the FDA in the post-approval period and identified at least 60 reports that Plaintiffs characterize as "opportunistic infections or potential opportunistic infections related to severe immunosuppression," and 163 reports that "could be considered serious opportunistic infections associated with severe immunosuppression" if more information were known. (¶¶ 163–64.) An August 29, 2005 article in the Wall Street Journal similarly concluded that Tysabri adverse event data received by the FDA included reports of "numerous" serious opportunistic infections as well as seven deaths from infections other than PML. (¶¶ 170–71.)

Plaintiffs also allege Defendants' knowledge and/or reckless disregard of opportunistic infections associated with Tysabri based on information obtained from various confidential sources.

Plaintiffs' Confidential Source No. 5 ("CS 5") is a neurologist who was "directly involved" with the Tysabri MS trials. (¶ 154.) CS 5 stated that several opportunistic infections occurred during the Tysabri MS and Crohn's disease trials, and specifically recalled three such infections. (¶ 154.) CS 5 said that Defendants had access to the data from MS trials and thus were "fully aware" of opportunistic infections that had occurred in both MS and Crohn's disease trials. (¶ 155.) CS 5 believes that these infections "constituted significant warnings" to Defendants about Tysabri's immunosuppressive risks. (¶ 154.) However CS 5 does not allege that either he or any other participant in the trials concluded that the data revealed a statistically significant causal relationship between any infections and Tysabri during his involvement with the Tysabri MS trials.

Plaintiffs' Confidential Source No. 4 ("CS 4") was a neurologist who participated in the MS Tysabri trials. (¶ 127.) CS 4 stated that senior management at Elan and Biogen were aware before February 28, 2005 "that Tysabri persisted in the body bound to lymphocytes for months after administration, leaving the patient vulnerable to opportunistic infections for a prolonged period, far longer than most immunosuppressive drugs." (¶ 127.) CS 4 also stated that (s)he had been informed of serious opportunistic infections in the Crohn's disease trials, and specifically mentioned two such infections. (¶ 155.)

Plaintiffs' Confidential Source No. 6 ("CS 6") was a neurologist involved in the SENTINEL Phase II MS trial. (¶ 157.) CS 6 reports that during the Tysabri clinical

trials, it became obvious that "continued use of Tysabri compromised the immune system" because, of the five participants in the trial who "contracted cancer," only one was in the placebo group. (¶ 157.) CS 6 recalled that one patient who received Tysabri developed malignant melanoma, "which was particularly unusual because MS patients do not typically get malignant melanoma," and another patient developed cervical cancer, which CS 6 claimed is caused by human polyomavirus, which is related to the JC virus that causes PML.[16] (¶ 157.)

Plaintiffs' Confidential Source No. 7 ("CS 7") was a data entry clerk who tracked clinical data for Biogen from May 2004 to December 2005. (¶ 158.) CS 7 estimated that fifty to sixty adverse events were reported on an average day during Tysabri MS trials and that this number increased to between sixty and seventy during June 2004 and just before approval in November 2004. (¶ 158.) Based on her experience with other clinical trials, CS 7 stated that these numbers were "extremely high." (¶ 158.) CS 7 stated that many of the adverse events in Tysabri trials were serious, and that some of the reports suggested symptoms of PML. (¶ 159.) CS 7 is "certain" that Defendants were aware of any concerns relating to the Tysabri clinical trials. (¶ 159.)

Plaintiffs' Confidential Source No. 2 ("CS 2"), a neurologist who worked with Tysabri at a Boston multiple sclerosis clinic, said that "there was a concern at Biogen that Tysabri might leave people unable to deal with other infections" and that the scientific team was generally aware of this concern. (¶¶ 78, 160.)

[16] Defendants point out in their opening brief that people in general do not develop malignant melanoma, and that information from the National Cancer Institute and the Centers for Disease Control indicate that cervical cancer is caused by the human papillomavirus, not the human polyomavirus. (Defs.' Br. 16 & n.7.)

### F. Defendants' alleged misstatements

Nearly fifty pages of Plaintiffs' Complaint are devoted to the identification of allegedly misleading statements and omissions made by Defendants during the Class Period.[17] These statements can be summarized as falling into several categories:

1. Statements regarding expected revenue from Tysabri sales and/or expected market share, for example, this excerpt from Elan's February 8, 2005 Press Release:

> Tysabri was approved in the U.S. as a treatment for all forms of relapsing remitting MS in late November 2004. While Elan expects Tysabri to become the market leader in this indication[,] it is too early in the launch to give revenue guidance for this product. However, on the basis of the initial take-up, Elan is optimistic of a return to profitability by the end of 2006.

(¶ 303; *see also, e.g.*, ¶¶ 253, 254, 272, 273, 293, 302–304.)

2. Statements indicating that Tysabri was a potential treatment for all MS patients without restriction, for example, Defendant Martin's statement during a May 13, 2004 conference call, "We think that [Tysabri] will clearly be positioned as mono-therapy, first line for MS on a global basis, period" (¶ 206), Defendant Martin's statement during a November 24, 2004 conference call, "We believe [Tysabri] will be a top line therapy for a disease that has a very high unmet medical need. The future growth in the marketplace is substantial both in the U.S. and particularly in Europe. . . ." (¶ 292), Defendant Ekman's statement

[17] Some of the allegedly misleading statements identified by Plaintiffs were statements made by Biogen employees. (*See, e.g.*, ¶¶ 262, 265, 287.) The Court assumes *arguendo* that Plaintiffs have adequately pled that these statements can be attributed to Defendants.

in a May 25, 2004 press release regarding Elan and Biogen's "continued commitment to providing a new treatment option for the more than one million patients experiencing the debilitating effects of MS" (¶ 212), and Defendant Ekman's statement that the two-year data from the AFFIRM trial "strengthen our belief that Tysabri will become the leading therapy for MS patients." (¶ 309). (*See also, e.g.*, ¶¶ 180, 221, 240, 262, 272, 291, 297, 308.)

3. Statements regarding Tysabri's safety profile, for example the statement in a February 18, 2004 Elan press release that "[s]erious adverse events have included infrequent hypersensitivity-like reactions" (¶ 179), Defendant Martin's statement during a May 13, 2004 conference call that Tysabri was "a product that's twice as efficacious at least as any current therapy with no side effect" (¶ 206), Defendants' statement in a May 25, 2004 Elan press release that "approximately 2,800 patients have received natalizumab in clinical trials, and the safety profile continues to support further development" (¶ 214), and Defendant Martin's representation during a January 11, 2005 conference call that, in the MS monotherapy trials, Tysabri "appears to be with all that we see, safe and very well tolerated. . . . [with] no opportunistic infections" (¶ 298; Aaron Decl. Ex. 18)[18]. (*See also, e.g.*, ¶¶ 189, 224, 235, 245, 261, 280, 281, 282, 289, 298, 307, 308.)

[18] Exhibit 18 to the Aaron Declaration is a transcript of the January 11, 2005 conference call quoted by Plaintiffs in the Complaint. (*See* ¶ 298.)

4. The certifications made pursuant to § 302 of the Sarbanes-Oxley Act of 2002 ("Sarbanes-Oxley Certifications") of defendants Cooke and Martin in Defendants' 2003 Form 20-F filing (filed April 19, 2004), which stated, *inter alia*, that the 2003 Form 20-F contained no material misrepresentations and that Elan maintained adequate internal controls to ensure that Elan management was made aware of material information required to be disclosed to the SEC. (¶¶ 201–04.)

5. Statements indicating that Defendants intended to market Tysabri as a monotherapy, not a combination therapy, for example, Defendant Martin's statement during a May 13, 2004 conference call, "We think that [Tysabri] will clearly be positioned as mono-therapy, first line for MS on a global basis, period." (¶ 206; *see also, e.g.*, ¶¶ 207, 210.)

6. Statements regarding the quality of Elan's research, for example, Defendant Martin's characterization of Elan's research capabilities as "world-class," "innovative," and "distinctive." (¶ 182.)

Plaintiffs do not attempt to explain why each individual statement is fraudulent, but allege generally that all of the statements identified by Plaintiffs are materially false and misleading for reasons listed in paragraph 188 of the Complaint. (*See, e.g.*, ¶¶ 188, 192, 204, 210, 218.) A summary of Plaintiffs' assertions in paragraph 188 is as follows: Defendants' statements were fraudulent because Defendants made statements about Tysabri without revealing (1) that Tysabri had "inherent" immunosuppressive effects, (2)

that Tysabri had caused "severe adverse events," including opportunistic infections and deaths; (3) that due to Tysabri's risks, it would be usable by a very limited MS patient population and would not generate revenue sufficient to return Elan to profitability; and (4) that Tysabri clinical trials did not include the necessary testing to detect symptoms of serious opportunistic infections.[19] (¶ 188.)

Plaintiffs also assert that Defendants' 2003 Form 20-F filing was materially misleading because (1) Defendants lacked the necessary controls to ensure that adverse events were reported to the FDA in a timely manner; (2) Defendants violated the Sarbanes-Oxley Act by submitting false certifications; and (3) Defendants violated Section 13(b)(2)(B) of the Securities Exchange Act by stating falsely that Elan maintained adequate internal controls. (¶ 204.)

## ANALYSIS

### I. Legal Standards

#### A. Standard for deciding a Rule 12(b)(6) motion to dismiss

Defendants have moved to dismiss Plaintiffs' Complaint pursuant to Rule 12(b)(6) of the Federal Rules of Civil Procedure. In considering a Rule 12(b)(6) motion to dismiss, a court is to accept as true all facts alleged in the complaint and draw all reasonable inferences in favor of the plaintiff. *Fernandez v. Chertoff,* 471 F.3d 45, 51 (2d Cir. 2006). However, the court may disregard a plaintiff's "legal conclusions, deductions

[19] Plaintiffs also allege that certain of Defendants' statements were fraudulent because they indicate Defendants' intent to market Tysabri as a monotherapy when in fact, "Elan and Biogen fully intended Tysabri to be used as a combination therapy." (¶ 210.) Plaintiffs do not pursue this claim in their opposition papers. In any event, because Plaintiffs allege no facts indicating that Defendants did not intend Tysabri to be marketed or used as a monotherapy, Plaintiffs do not state a claim for securities fraud on this basis.

or opinions couched as factual allegations." *See, e.g., In re NYSE Specialists Sec. Litig.*, 503 F.3d 89, 95 (2d Cir. 2007). The court is also not required to credit conclusory statements unsupported by factual allegations. *See, e.g., Otor, S.A. v. Credit Lyonnais, S.A.*, No. 04 Civ. 6978, 2006 WL 2613775, at *2 (S.D.N.Y. Sept. 11, 2006); *see also Davey v. Jones*, No. 06 Civ. 4206, 2007 WL 1378428, at *2 (S.D.N.Y. May 11, 2007) ("[B]ald contentions, unsupported characterizations, and legal conclusions are not well-pleaded allegations, and will not suffice to defeat a motion to dismiss.").

The Court is generally limited to "the factual allegations in [the] complaint, documents attached to the complaint as an exhibit or incorporated in it by reference, matters of which judicial notice may be taken, or documents either in plaintiff['s] possession or of which plaintiff[] had knowledge and relied on in bringing suit." *Brass v. Am. Film Techs., Inc.*, 987 F.2d 142, 150 (2d Cir. 1993). "The court need not accept as true an allegation that is contradicted by documents on which the complaint relies." *In re Bristol-Myers Squibb Sec. Litig.*, 312 F. Supp. 2d 549, 555 (S.D.N.Y. 2004); *Rapoport v. Asia Elecs. Holding Co.*, 88 F. Supp. 2d 179, 184 (S.D.N.Y. 2000) ("If these documents contradict the allegations of the amended complaint, the documents control.").

**B. Pleading requirements for Section 10(b) and Rule 10b-5 claims**

To state a claim for securities fraud under Section 10(b) of the 1934 Act and SEC Rule 10b-5, a plaintiff must allege that the defendant: "(1) made misstatements or omissions of material fact; (2) with scienter; (3) in connection with the purchase or sale of securities; (4) upon which plaintiffs relied; and (5) that plaintiffs' reliance was the proximate cause of their injury." *In re IBM Corp. Sec. Litig.*, 163 F.3d 102, 106 (2d Cir. 1998).

Claims of securities fraud are subject to heightened pleading requirements imposed by Fed. R. Civ. P. 9(b) and the Private Securities Litigation Reform Act ("PSLRA"), 15 U.S.C. § 78u-4. *ATSI Commc'ns, Inc. v. Shaar Fund, Ltd.*, 493 F.3d 87, 99 (2d Cir. 2007). Rule 9(b) requires that the "circumstances constituting fraud . . . shall be stated with particularity." Fed. R. Civ. P. 9(b). Thus, the Second Circuit has instructed that a "securities fraud complaint based on misstatements must (1) specify the statements that the plaintiff contends were fraudulent, (2) identify the speaker, (3) state where and when the statements were made, and (4) explain why the statements were fraudulent." *ATSI Commc'ns, Inc.*, 493 F.3d at 99. "[D]istorted inferences and speculations" do not satisfy the pleading requirements of Rule 9(b). *Segal v. Gordon*, 567 F.2d 602, 606–08 (2d Cir. 1972).

Similarly, the PSLRA requires that a complaint alleging misleading statements or omissions "shall specify each statement alleged to have been misleading, the reason or reasons why the statement is misleading, and, if an allegation regarding the statement or omission is made on information and belief, the complaint shall state with particularity all facts on which that belief is formed." 15 U.S.C. § 78u-4(b)(1). For securities claims that require scienter, the complaint must also "state with particularity facts giving rise to a strong inference that the defendant acted with the required state of mind." *Id.* § 78u-4(b)(2). The Supreme Court has recently instructed that a complaint should survive a Rule 12(b)(6) motion to dismiss "only if a reasonable person would deem the inference of scienter cogent and at least as compelling as any opposing inference one could draw from the facts alleged." *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 127 S. Ct. 2499, 2510 (2007).

If a plaintiff in a securities fraud action attempts to support its claim that a defendant made material misstatements or omissions by using the accounts of confidential sources, the PSLRA requires these sources to be "described in the complaint with sufficient particularity to support the probability that a person in the position occupied by the source would possess the information alleged." *Novak v. Kasaks*, 216 F.3d 300, 314 (2d Cir. 2000). The Third Circuit has adopted the *Novak* approach and identified the following factors as relevant to a determination whether allegations regarding a confidential source meet the PSLRA's particularity requirement: "the detail provided by the confidential sources, the sources' basis of knowledge, the reliability of the sources, the corroborative nature of other facts alleged, including from other sources, the coherence and plausibility of the allegations, and similar indicia." *Cal. Pub. Employees' Ret. Sys. v. Chubb Corp.*, 394 F.3d 126, 147 (3d Cir. 2004).

**C. Section 20(a) liability**

Under § 20(a) of the 1934 Act, "a controlling person is jointly and severally liable with a controlled person to any person to whom the controlled person is liable 'unless the controlling person acted in good faith and did not directly or indirectly induce the act or acts constituting the violation or cause of action.'" *Boguslavsky v. Kaplan*, 159 F.3d 715, 720 (2d Cir. 1998) (quoting 15 U.S.C. § 78t(a)). "In order to establish a *prima facie* case of liability under § 20(a), a plaintiff must show: (1) a primary violation by a controlled person; (2) control of the primary violator by the defendant; and (3) 'that the controlling person was in some meaningful sense a culpable participant' in the primary violation." *Id.* (quoting *SEC v. First Jersey Sec., Inc.*, 101 F.3d 1450, 1472 (2d Cir.1996), *cert. denied*, 522 U.S. 812 (1997)).

## II. Defendants' alleged misrepresentations regarding Tysabri's safety profile

### A. Materiality

Plaintiffs allege that all of the identified Class Period statements were materially false and misleading for eight reasons listed in paragraph 188 of the Complaint, all of which relate to immune-related safety issues associated with Tysabri and/or the consequences of these safety issues for Tysabri marketability and sales. In essence, Plaintiffs argue in paragraph 188 that Defendants engaged in securities fraud by making public statements about Tysabri and its market potential without disclosing information regarding the risk of PML and other "serious opportunistic infections" associated with the drug. (*See, e.g.,* ¶ 188.)

There is no question that Defendants represented that Tysabri clinical trials had revealed no significant safety issues, that Tysabri would be usable by a broad MS patient population, and that Tysabri had the potential to be a "blockbuster" drug. Indeed, Defendants made specific statements regarding the lack of known side effects associated with the drug. For example, Martin reported in May 2004 that the data from Phase II MS clinical trials indicated "no side effect[s]" (¶ 206), and in January 2005, with respect to safety data from Tysabri MS monotherapy trials, that "Tysabri appears to be, with all that we see, safe and very well tolerated. . . . no opportunistic infections" (¶ 298).

By choosing to speak about the safety of Tysabri, Defendants assumed a duty to disclose material information regarding adverse events. *See, e.g., Caiola v. Citibank, N.A., New York*, 295 F.3d 312, 331 (2d Cir. 2002) ("[U]pon choosing to speak, one must speak truthfully about material issues."). Therefore, a defendant's failure to disclose information may constitute an omission in violation of the securities laws if the omitted

information is material and "necessary to make another statement not misleading." 17 C.F.R. § 240.10b-5(b).

Information is material for the purposes of Section 10(b) and Rule 10b-5 if there is "a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information made available." *Basic Inc. v. Levinson*, 485 U.S. 224, 231–32 (1988). Because "[m]ateriality is a mixed question of law and fact. . . . a complaint may not properly be dismissed . . . on the ground that the alleged misstatements or omissions are not material unless they are so obviously unimportant to a reasonable investor that reasonable minds could not differ on the question of their importance." *Ganino v. Citizens Utils. Co.*, 228 F.3d 154, 162 (2d Cir. 2000).

The Second Circuit has stated that information regarding a drug's adverse effects does not become material until that information "provide[s] statistically significant evidence that the ill effects may be caused by—rather than randomly associated with—use of the drugs and are sufficiently serious and frequent to affect future earnings." *In re Carter-Wallace Sec. Litig.* (*Carter-Wallace I*), 150 F.3d 153, 157 (2d Cir. 1998); *see also In re Carter-Wallace Sec. Litig.* (*Carter-Wallace II*), 220 F.3d 36, 41 ("Carter-Wallace had no sound reason to doubt the commercial viability of Felbatol or the value of its inventory until the reports of Felbatol-associated deaths became statistically significant.")

In *Carter-Wallace I*, the plaintiffs alleged violations of Section 10(b) and Rule 10(b)(5) based on defendant drug manufacturer Carter-Wallace's allegedly misleading statements regarding adverse events associated with its epilepsy drug Felbatol. *Carter-Wallace I*, 150 F.3d at 154. The drug was introduced in August 1993 and promoted

through July 1994 as having an "unprecedented safety profile." *Carter-Wallace II*, 220 F.3d at 38. In 1994, Carter-Wallace began receiving reports of deaths from aplastic anemia, a bone marrow disease, in patients taking Felbatol. *Carter-Wallace I*, 150 F.3d at 155. Carter-Wallace received one such report in January, another in March, two reports in April, two reports in May, and four reports in July. *Id.* On August 1, 1994, Carter-Wallace issued a "Dear Doctor" letter recommending that most patients discontinue Felbatol treatment. *Id.* The Second Circuit upheld the district court's dismissal of plaintiffs' Section 10(b) claims, stating that information regarding the aplastic anemia deaths did not become material until "Carter-Wallace had information that Felbatol had caused a statistically significant number of aplastic-anemia deaths and therefore had reason to believe that the commercial viability of Felbatol was threatened." *Id.* at 157. Therefore, the court held that Carter-Wallace was under no duty to disclose the Felbatol-related deaths prior to its announcement on August 1, 1994. *Id.*

Alleged nondisclosure of information regarding adverse drug events was also addressed by *In re Bayer AG Securities Litigation*, No. 03 Civ. 1546, 2004 WL 2190357 (S.D.N.Y. Sept. 30, 2004). The adverse event at issue in this case was a condition known as rhabdomyolysis, which involves the acute breakdown of muscle tissue. *Id.* at *2. In May 1998, Bayer was aware of four cases of rhabdomyolysis in patients taking Baycol. *Id.* In 1998 and 1999, Bayer started receiving reports of rhabdomyolysis in patients taking Baycol in combination with a drug called gemfibrozil. *Id.* By April 1999, Bayer had received fifty-one adverse event reports regarding rhabdomyolysis in patients taking Baycol and subsequently received sixty such reports in the last two months of the year. *Id.* at *3–4. On March 10, 2000, a Bayer epidemiologist concluded that the risk of

rhabdomyolysis associated with Baycol was considerably greater that associated with other drugs of its class and that Baycol users were at a "remarkable disadvantage" relative to patients taking these other drugs. *Id.* at *4. Finally, at a meeting in August 2000, Bayer's drug safety executives reached a consensus that the potential dangers associated with Baycol were "putting the brand at risk." *Id.* at *4, 10.

The *Bayer* court stated that while *Carter-Wallace I* holds that isolated adverse event reports, lacking statistical significance, cannot establish that a drug is unsafe, it does not address whether such reports, supplemented by other evidence, might suffice. *Id.* at *9. In light of this, the district court held that Bayer's duty to disclose information regarding the rhabdomyolysis reports arose after the August 2000 meeting because, even if causation had not been established at this time, it could be inferred that defendants viewed these issues as "sufficiently serious and frequent to affect future earnings." *Id.* at *10 (quoting *Carter-Wallace I*, 150 F.3d at 157). However, there was no duty to disclose this informationbefore the consensus emerged that the rhabdomyolysis issue was putting the brand at risk. *Id.*

Decisions from other courts addressing similar Section 10(b) claims are generally consistent with *Carter-Wallace I.* In *Oran v. Stafford*, 226 F.3d 275 (3d Cir. 2000), the Third Circuit affirmed the district court's dismissal of plaintiffs' securities fraud claims, finding that twenty-four reports of heart valve abnormalities in patients using drug combination known as "fen-phen" "suggest[ed] a link" between the adverse events and the drug but did not establish a statistically significant or "medically conclusive" relationship. 226 F.3d at 279–80, 282–84. Therefore, these reports were not material, either alone or in combination with thirty-one similar reports in European fen-phen users.

*Id.* at 279–80, 283–84 ("[P]laintiffs never clearly explain how the accumulation of additional anecdotal data, short of the point of statistical significance, would have added anything to the disclosure [of inconclusive adverse event data].") In *In re Intrabiotics Pharmaceuticals, Inc. Securities Litigation*, No. C 04-02675, 2006 WL 708594, (N.D. Cal. Jan. 23, 2006), the plaintiffs' complaint alleged a Section 10(b) violation based on the defendants' representation that their drug was "safe and well-tolerated" in clinical trials. 2006 WL 708594, at *11–12. The court dismissed this claim in part because plaintiffs did not allege at what point during the clinical trials it would have been apparent that the drug was causing the adverse events at issue or when defendants became aware of this information. *Id.*[20]

Though *Carter-Wallace I* and *Bayer* combined materiality and scienter into a single inquiry, the *Carter-Wallace I* holding has implications for both elements. With respect to materiality, it stands for the proposition that isolated adverse event reports are not generally material unless and until (1) they provide evidence of an actual (*i.e.*, statistically significant) correlation between the adverse event and the drug, and (2) the adverse events at issue are "sufficiently serious and frequent to affect future earnings." *Carter-Wallace I*, 150 F.3d at 157. However, this Court agrees with the *Bayer* court that *Carter-Wallace I* does not establish a bright-line rule for the materiality of information regarding drug safety risks. Instead, this type of information may become material even

[20] *See also In re GlaxoSmithkline PLC Sec. Litig.*, No. 05 Civ. 3751, 2006 WL 2871968, at *10 (S.D.N.Y. Oct. 6, 2006) (granting motion to dismiss, finding alleged adverse events not to be material because they potentially affected only a "nominal amount of off-label sales," which "certainly did not threaten the commercial viability of the drug."); *In re Alliance Pharm. Corp. Sec. Litig.*, 279 F. Supp. 2d 171, 189 (S.D.N.Y. 2003) (rejecting plaintiffs' argument that "any undesirable results that arise during clinical testing are necessarily material," citing *Carter-Wallace I*); *but see In re Regeneron Pharms. Inc. Sec. Litig.*, No. 03 Civ. 3111, 2005 WL 225288, at *8–9, 19–21 (S.D.N.Y. Feb. 1, 2005) (denying motion to dismiss Section 10(b) claims alleging misstatements regarding side effects associated with the drug without specifying the allegedly undisclosed side effects and without reference to *Carter-Wallace I*).

in the absence of statistically significant evidence in light of other indications that the risk associated with adverse drug events is legitimate and serious enough to threaten drug sales.

**1. PML**

With respect to PML, Plaintiffs' allegations indicate only that, between February 7, 2005 and February 28, 2005, Defendants learned that one or two patients receiving Tysabri had developed PML. Plaintiffs do not allege any other diagnosis of PML during the Class Period.[21]

Plaintiffs do not allege that the information available to Defendants during the Class Period constituted evidence of a statistically significant relationship between Tysabri and PML. While Dr. Panzara reported at the March 2006 FDA hearing that "[Tysabri] treatment is associated with an increased risk of PML" (Aaron Decl. Ex. 5 at 65), it hardly follows that this relationship was established before PML was first diagnosed in a Tysabri user in February 2005.

Under *Carter-Wallace I*, reports regarding PML did not become material until they constituted "statistically significant evidence that the ill effects may be caused by—rather than randomly associated with—use of the drugs and are sufficiently serious and frequent to affect future earnings." 150 F.3d at 157. Plaintiffs do not allege that Defendants failed to disclose any material information regarding a causal relationship between Tysabri and PML prior to February 28, 2005. Obviously, the fact that Tysabri sales would be suspended indefinitely was material and had to be disclosed by Defendants in a timely manner. However, as discussed *infra*, Plaintiffs make no

[21] Plaintiffs allege that a Biogen officer, Thomas Bucknum, learned that one patient in a Tysabri trial had been diagnosed with PML on February 18, 2005. (¶ 344.)

allegations regarding when Defendants made this decision, nor do they allege facts indicating that Defendants concealed this decision or the underlying PML diagnoses from investors.

### 2. Non-PML opportunistic infections

#### a. Data regarding non-PML opportunistic infections

Plaintiffs allege that Defendants knew, before Defendants applied for fast-track approval for Tysabri, that serious non-PML opportunistic infections and deaths had occurred during Tysabri clinical trials (*see, e.g.*, ¶¶ 5, 130, 153–54), and that these infections continued to be reported after FDA approval (*see, e.g.*, ¶¶ 162–64, 171). Plaintiffs do not allege the existence of evidence demonstrating a statistically significant connection between non-PML opportunistic infections and Tysabri, either during the Class Period or at any other time.

The data regarding infections reported at the March 2006 FDA Hearing are inconclusive at best. At the March 2006 FDA Hearing, Dr. Panzara stated that there "*may* also be an increased risk of other opportunistic infections." (Aaron Decl. Ex. 5 at 65 (emphasis added).) Dr. Hughes reported a similar incidence of serious infections and overall infections in Tysabri- and placebo-treated subjects in MS trials, a similar incidence of serious infections in the two groups in Crohn's disease trials, and a slightly increased incidence of overall infections in Tysabri subjects (40% in Tysabri subjects vs. 36% in placebo subjects) in Crohn's disease trials. (*Id.* Ex. 5 at 161–63.) Dr. Panzara reported a "slight" 1.1% increase in herpes infections in Tysabri-treated subjects in MS clinical trials, largely attributable to data from the combination therapy trial,[22] and a

[22] The incidence of herpetic infections in the monotherapy study was 6.4% in Tysabri subjects and 6.0% in placebo subjects. (Aaron Decl. Ex. 5 at 59.) The incidence of herpetic infections in the combination trial

smaller 0.5% increase in herpes infections in Tysabri subjects in Crohn's disease trials. (*Id.* Ex. 5 at 59–60.) Even assuming these data indicate a significant increase in non-PML opportunistic infections in Tysabri patients, Plaintiffs allege no facts indicating that this information existed during the Class Period. Indeed, Plaintiffs, in alleging that Defendants' Class Period statements were misleading because Tysabri clinical trials "failed to include the full range of medical tests necessary to timely detect symptoms of serious opportunistic infections," apparently acknowledge that these infections were *not* diagnosed or known at the relevant time. (¶ 188.)

Plaintiffs' allegations regarding adverse event reports of "opportunistic infections," "potential opportunistic infections," and "severe infections . . . that could be opportunistic infections" in patients who had received Tysabri while it was on the market describe individual adverse event reports that do not rise to the level of material information under *Carter-Wallace I.* (¶¶ 162–64.) These reports suggest only that these adverse events occurred, not that they reflected any meaningful or statistically significant relationship to Tysabri at that time (or, indeed, subsequently). The adverse events identified by Plaintiffs are of particularly limited value because they do not even distinguish between actual opportunistic infections and "potential" opportunistic infections (whatever that might mean). As a result, it is not clear how many of these, if any, were or should have been classified as opportunistic infections by Elan.[23]

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was 8.4% in subjects receiving Tysabri and Avonex and 6.1% in subjects receiving placebo and Avonex. (*Id.* Ex. 5 at 59–60.)

[23] Notably, Dr. Panzara stated that no opportunistic infections were reported during the three months that Tysabri was on the market. (Aaron Decl. Ex. 5 at 56–57.) Plaintiffs do not allege that this statement was false.

Plaintiffs allege that there were two deaths in Tysabri subjects from non-PML opportunistic infections and that various types of non-PML opportunistic infections occurred during the clinical trials.[24] Plaintiffs' confidential sources also report that opportunistic infections occurred during the clinical trials, but do not reveal whether these infections occurred in patients receiving Tysabri, much less whether the opportunistic infections were caused by Tysabri rather than the subject's underlying condition, other medications being taken, or even chance. *See In re Bayer AG*, 2004 WL 2190357, at *3 ("The FDA offers a series of caveats regarding the unreliability of adverse event reports: (1) because the reports are submitted voluntarily, they contain information that 'has not been scientifically or otherwise verified'; (2) the reported condition may not result from the drug but from 'the underlying disease for which the drug was given,' other medications being taken, or even 'by chance'; and (3) 'accumulated case reports cannot be used to calculate incidence or estimates of drug risk.'"). These allegations, even if accepted as true, are tantamount to adverse event reports and provide no indication that opportunistic infections are "caused by—rather than randomly associated with—" Tysabri. *Carter-Wallace I*, 150 F.3d at 157.[25]

Moreover, Plaintiffs also do not allege facts indicating that the risk of non-PML opportunistic infections from Tysabri was "sufficiently serious . . . to affect future

[24] While Plaintiffs allege that Dr. Panzara disclosed eleven types of opportunistic infections that occurred during Tysabri trials, this allegation is contradicted by the transcript of the March 2006 FDA Hearing that Plaintiffs repeatedly cite in their Complaint. At the hearing, Dr. Panzara described six types of opportunistic infections in Tysabri subjects. (*Compare* ¶ 144 *with* Aaron Decl. Ex. 5 at 61–65.) And while Dr. Panzara reported that Tysabri was associated with an increased risk of PML, he stated only that there "may also be an increased risk of other opportunistic infections." (Aaron Decl. Ex. 5 at 65.) Furthermore, these statements were made in March 2006 after detailed study and there are no allegations that Defendants reached such conclusions during the Class Period.

[25] There were many more subjects in the Tysabri group than in the placebo group in the clinical trials. (*See* Aaron Decl. Ex. 17 at 8 (reporting 2,539 Tysabri subjects and 1,391 placebo subjects).) Therefore, even if Plaintiffs had alleged that there were more adverse events in Tysabri patients, this would not necessarily be a meaningful difference.

earnings." *Carter-Wallace I*, 150 F.3d 153, 157 (2d Cir. 1998); *In re GlaxoSmithkline PLC Sec. Litig.*, No. 05 Civ. 3751, 2006 WL 2871968, at *10 (S.D.N.Y. Oct. 6, 2006) ("In order to be material, a pharmaceutical company's failure to disclose information about a drug must be of sufficient magnitude that the commercial viability of the drug would be called into question if the truth were disclosed."). The press release announcing the suspension of Tysabri sales mentions only the two cases of PML in Tysabri MS trials; it does not mention any other opportunistic infection. (¶ 318.)

**b. "Red flags"**

Plaintiffs argue that the alleged "red flags" it has identified distinguish this case from *Carter-Wallace I* because they allegedly put Defendants on notice that Tysabri was likely to produce immunosuppressive effects in patients. Therefore, the Court must also consider whether any of the alleged "red flags" might, in combination with the adverse event reports, could constitute material information. They could not.

The allegedly "unexplained deaths" in animal studies of Tysabri did not suggest anything about Tysabri's immunosuppressive effects or its potential to promote opportunistic infections. Only pure speculation supports an inference that these deaths were related to immunosuppression, or, indeed that they were caused by anything other than the causes to which they were attributed at the time. (*See* ¶ 112.)

Plaintiffs allege no facts indicating that Defendants were aware of any of the alleged warnings by Dr. Steinman, Dr. Miller, and others regarding Tysabri's immunosuppressive effects. However, even accepting Plaintiffs' contention that Defendants can be charged with knowledge of "all facts and information" concerning

Tysabri (¶ 107), these alleged warnings in the scientific literature would not have lowered the threshold at which reports of opportunistic infections became material.

At best, the "red flags" in the literature identified a particular category of adverse events that scientists believed Tysabri might produce. The risk that Tysabri would in fact have these effects was merely part of the inherent risk, understood by investors, that Tysabri, like any drug at the development stage, might fail to live up to expectations due to safety or efficacy issues that emerge during clinical trials. Indeed, the very purpose of the FDA-mandated clinical trials is to establish whether a drug is safe and effective for its intended use. Contrary to Plaintiffs' assertions, the warnings did not put Defendants on notice that Tysabri was "certain to cause . . . serious and sometimes life-threatening opportunistic infections." (*See, e.g.*, ¶ 130.) Even if scientists suspected that Tysabri might cause severe adverse events and Defendants knew of these suspicions, these facts would not have required Defendants to conclude that these effects were real before such a relationship was established using accepted statistical methods and standards of proof. *Cf. Carter-Wallace II*, 220 F.3d at 42 ("[T]he early medical reports may have indicated a potential problem, but until a connection between Felbatol and any illness could be made, we would not expect Carter-Wallace to abandon its product on what, at the time, would have been speculation.").

Furthermore, because actual adverse event reports are not material unless statistically significant, mere warnings or predictions regarding the occurrence of these adverse events must be immaterial as well. The alleged warnings identified by Plaintiffs were hypotheses, not evidence, and did not change the likelihood that actual adverse event reports represented a meaningful association. Therefore, the combination of these

alleged warnings and the adverse event reports are not cumulatively more material than the adverse event reports standing alone. *See, e.g., Oran v. Stafford*, 226 F.3d at 284 ("[P]laintiffs never clearly explain how the accumulation of additional anecdotal data, short of the point of statistical significance, would have added anything to the disclosures already made . . . . [T]he aggregate of available information would nevertheless have led a reasonable investor to the same conclusion—that the relationship . . . was still inconclusive.").

Plaintiffs also argue that this case should be distinguished from *Carter-Wallace I* because "Tysabri is known to be inherently immunosuppressive by its mechanism of action" while in *Carter-Wallace I* and *Bayer*, "the adverse events were unrelated to how the drug inherently worked." (Pls.' Opp'n Defs.' Mot. Dismiss Consol. Class Action Compl. Viol. Fed. Sec. Laws ("Pls.' Opp'n Br.") 24 n.21.) That is, "unlike in [*Carter-Wallace I*], the opportunistic infections caused by Tysabri were precisely the type of infections that Defendants would have expected because such infections only occur in individuals with severely compromised immune systems, which goes to the very heart of the way Tysabri works." (*Id.* at 27 n.22.) As a result, Plaintiffs contend that "even one opportunistic infection is significant enough to place Tysabri's safety and marketability in question." (*Id.* at 24 n.21).

The Court interprets Plaintiffs' argument as follows: Because Tysabri was believed to treat MS by inhibiting a component of the immune system, reports of adverse events related to the suppression of the immune system, like opportunistic infections, were expected and therefore more likely to be causally, as opposed to randomly,

associated with Tysabri. (*Id.* at 24 n.21, 27 n.22.) Plaintiffs cite no case law in support of their proposed distinction, nor do they explain why such a distinction makes sense.

The *Carter-Wallace I* holding was not based on Felbatol's mechanism of action or on whether aplastic anemia was an expected or unexpected consequence of Felbatol use. Even accepting the doubtful premise that Defendants should have expected opportunistic infections in Tysabri users, Plaintiffs' attempted distinction does not address the rationale behind the *Carter-Wallace I* holding—that information regarding adverse events does not become material until the accumulation of sufficient evidence to show that the events are actually, not just randomly, associated with the drug. The fact that an adverse effect might be biologically plausible based on a drug's known mechanism of action does not affect the necessity to confirm that a real association exists.

For the foregoing reasons, the Court finds that Plaintiffs' allegations are insufficient to state a claim for securities fraud based on Defendants' failure to disclose information regarding the risk of non-PML opportunistic infections associated with Tysabri. Such risks did not become material until a causal link was established and neither opinion and speculation as to the degree of such risk nor the existence of adverse event reports were in themselves material. Plaintiffs do not allege facts that, if proven, would support an inference that a causal relationship between Tysabri and non-PML opportunistic infections was established but not disclosed during the Class Period. Nor do Plaintiffs allege facts that, if proven, would establish that a causal association between Tysabri and non-PML opportunistic infections would impact the expected financial return from the drug. *See Carter-Wallace I*, 150 F.3d at 157 ("Drug companies need not disclose isolated reports of illnesses suffered by users of their drugs until those reports

provide statistically significant evidence that the ill effects may be caused by-rather than randomly associated with-use of the drugs and are sufficiently serious and frequent to affect future earnings.")[26]

**B. Plaintiffs do not adequately allege scienter**

A plaintiff in a Rule 10b-5 action must also plead that the defendant acted with scienter in making the materially misleading statement or omission. Scienter in this context means "intent to deceive, manipulate, or defraud, or reckless conduct." *ATSI Commcn's, Inc. v. Shaar Fund, Ltd.*, 493 F.3d 87, 99 (2d Cir. 2007).

The PSLRA requires Plaintiffs to plead facts sufficient to raise a "strong inference" of scienter. 15 U.S.C. § 78u-4(b)(2). In *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 127 S. Ct. 2499 (2007), the Supreme Court clarified that a "strong inference" is an inference that is "at least as likely as any plausible opposing inference." 127 S. Ct. at 2513. Therefore, "the court must take into account plausible opposing inferences" and consider whether a "reasonable person would deem the inference of scienter cogent and at least as compelling as any opposing inference one could draw from the facts alleged."

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[26] Plaintiffs' Complaint also includes numerous allegations regarding malignancies and tumors reported in Tysabri clinical trials or post-marketing adverse event reports. (*See, e.g.*, ¶¶ 112, 143, 148, 157, 159, 165.) Plaintiffs do not assert in their Complaint that any of Defendants' statements were misleading due to a failure to disclose any information about carcinogenicity, nor do Plaintiffs mention these allegations in their opposition brief. Nevertheless, the Court will briefly address these allegations.

The fact that malignancies and/or tumors may have been reported in Tysabri users is not material information under *Carter-Wallace I*. Plaintiffs do not allege any association, much less a statistically significant association, between these events and Tysabri, and do not allege that anyone at Elan or Biogen knew of or was concerned about such an association during the Class Period. At the March 2006 FDA Hearing, Dr. Alice Hughes of the FDA noted that carcinogenicity was at least "a theoretical concern" in Tysabri users because Tysabri disrupts trafficking of cells responsible for tumor immunosurveillance in the body. (Aaron Decl. Ex. 5 at 175.) However, she stated that there was no increase in malignancies in the Tysabri group in MS trials (*id.* Ex. 5 at 182), and described a slight increase in malignancies observed in the Tysabri group in Crohn's disease trials as biologically implausible given the small number of infusions received (*id.* Ex. 5 at 176).

The allegations regarding malignancies and tumors might also be interpreted as another "red flag" regarding Tysabri's immunosuppressive potential. However, this "red flag," like the others, does not affect the materiality of information regarding PML or other opportunistic infections because mere predictions regarding the plausibility of immune-related adverse events do not constitute evidence that such events are actually associated with the drug.

*Id.* at 2510. In making this determination, the court should not "scrutinize each allegation in isolation" but should consider the inference created by the allegations of the complaint as a whole. *Tellabs*, 127 S. Ct. at 2511. In sum, the ultimate question for the court in determining whether a plaintiff has adequately pled scienter is, "When the allegations are accepted as true and taken collectively, would a reasonable person deem the inference of scienter at least as strong as any opposing inference?" *Tellabs*, 127 S. Ct. at 2511.

In the Second Circuit, a plaintiff may satisfy the scienter pleading requirements with allegations (1) showing that the defendants had both motive and opportunity to commit the fraud or (2) constituting strong circumstantial evidence of conscious misbehavior or recklessness. *See, e.g., ATSI Commc'ns, Inc.*, 493 F.3d at 99.

**1. Motive and opportunity**

Plaintiffs argue that they have sufficiently alleged that Defendants possessed "motive and opportunity" to commit fraud and that these allegations support an inference of scienter. (Pls.' Opp'n Br. 30–33.) Plaintiffs make three allegations to support a showing of "motive": (1) that Elan needed Tysabri to be profitable in order to avoid bankruptcy (¶¶ 6, 384–88), (2) that Elan needed to conceal negative information about Tysabri in order to complete a $1.15 billion senior notes offering used to fund development of Tysabri (¶¶ 7, 389–92), and (3) that the Individual Defendants were motivated to inflate Elan stock price in order to maximize year-end bonuses tied to Elan's financial performance. (¶¶ 393–98). Defendants clearly had opportunity to commit fraud and do not dispute this point. *See, e.g., Pension Comm. of Univ. of Montreal Pension Plan v. Banc of Am. Sec., LLC*, 446 F. Supp. 2d 163, 181 (S.D.N.Y. 2006). ("Regarding

the 'opportunity' prong, courts often assume that corporations, corporate officers, and corporate directors would have the opportunity to commit fraud if they so desired.").

To support an inference of scienter, motive allegations must identify "concrete benefits that could be realized by one or more of the false statements and wrongful nondisclosures alleged." *Kalnit v. Eichler*, 264 F.3d 131, 139 (2d Cir. 2001). "Motives that are generally possessed by most corporate directors and officers do not suffice; instead, plaintiffs must assert a concrete and personal benefit to the individual defendants resulting from the fraud. Insufficient motives . . . include (1) the desire for the corporation to appear profitable and (2) the desire to keep stock prices high to increase officer compensation." *Id.* at 139; *see also Acito v. IMCERA Group, Inc.*, 47 F.3d 47, 54 (2d Cir. 1995) ("[T]he existence, without more, of executive compensation dependent upon stock value does not give rise to a strong inference of scienter."); *Greene v. Hanover Direct, Inc.*, No. 06 Civ. 13308, 2007 WL 4224372, at *4 (S.D.N.Y. Nov. 19, 2007) (finding "prospect of maximizing [executives'] year-end bonuses" to be insufficient basis for allegation of scienter).

Any corporation would be motivated to make a profit, to avoid bankruptcy, or to finance the successful launch of a promising product. Similarly, corporate executives are generally motivated to maximize bonus compensation. These allegations do not support an inference of scienter.

### 2. Circumstantial Evidence of Conscious Misbehavior or Recklessness

Plaintiffs also argue that an inference of scienter is supported by the following allegations of "strong circumstantial evidence of [Defendants'] conscious misbehavior or recklessness": (1) Defendants' "actual knowledge" and "reckless disregard" of safety

issues associated with Tysabri (Pls.' Opp'n Br. 25–29); (2) Defendants' "pattern" of past fraudulent conduct (*id.* at 29); and (3) Defendants' "deliberate scheme to conceal serious opportunistic infections from the FDA" (*id.* at 29–30).

**a. Defendants' knowledge regarding Tysabri and PML**

Plaintiffs do not allege facts indicating that Defendants knew about and failed to timely disclose any information about PML during the Class Period. Plaintiffs therefore do not raise a strong inference that Defendants acted with scienter in failing to disclose information regarding a link between PML and Tysabri.

Plaintiffs allege no facts supporting an inference that Defendants knew prior to February 2005 that any Tysabri user had developed PML. Plaintiffs' allegations indicate only that, between February 7, 2005 and February 28, 2005, Defendants learned that one or two patients receiving Tysabri had developed PML, and that Defendants decided to withdraw Tysabri from the market in light of this information. Plaintiffs do not allege that PML was diagnosed in any Tysabri user before this time.

While Plaintiffs allege that two patients had exhibited symptoms of PML in late 2004,[27] they do not allege that anyone attributed these symptoms to PML before February 2005. The allegation regarding the occurrence of PML in October 2004 is based on a February 28, 2005 letter to doctors and testimony at the March 2006 FDA hearing. (¶¶ 312, 317.) A review of the FDA hearing transcript indicates that no diagnosis of PML was made at the time because the patient's symptoms were consistent with and attributed to MS (*see, e.g.*, Aaron Decl. Ex. 5 at 77, 150), and that it can be difficult to distinguish the symptoms of the two conditions (*see, e.g.*, Aaron Decl. Ex. 5 at 69, 77, 95,

[27] According to the documents Plaintiffs rely upon, one patient's symptoms first appeared in October 2004 (Aaron Decl. Ex. 5 at 151); the other first displayed symptoms of PML in November 2004 (*id.* Ex. 5 at 150).

150.). Dr. Susan McDermott, an FDA neurologist, specifically stated that, in the case of one patient, "PML was not thought of as a possibility" in October 2004. (*See, e.g.*, Aaron Decl. Ex. 5 at 151–52.)

Plaintiffs allege that confidential sources CS 8 and CS 9 expressed doubts that any competent neuropathologist could have misdiagnosed the third reported PML case as malignant astrocytoma in July 2003. These allegations simply confirm that this individual was not diagnosed with PML at that time, consistent with Dr. McDermott's testimony at the March 2006 FDA hearing that PML was diagnosed in this individual only after a retrospective analysis. (Aaron Decl. Ex. 5 at 154.) CS 8's suspicions of foul play fall far short of a sufficient allegation of an effort by Defendants "to conceal the true diagnosis." (¶ 167.)

The assertion of CS 7, a data entry clerk who worked on Tysabri MS trials, that numerous complaints during the Tysabri clinical trials "suggested symptoms of PML" is disregarded because CS 7 was not a physician but a data entry clerk, and Plaintiffs allege no facts indicating that CS 7 was qualified to make this or any medical diagnosis. *See, e.g., Novak v. Kasaks*, 216 F.3d 300, 314 (2d Cir. 2000) (holding that confidential sources must be "described in the complaint with sufficient particularity to support the probability that a person in the position occupied by the source would possess the information alleged.") In any case, this information would not affect the Court's analysis because neither Plaintiffs nor CS 7 allege that anyone attributed these symptoms to PML at the time.

Because Plaintiffs do not allege that PML was diagnosed in Tysabri users before February 7, 2005, the Court finds that Plaintiffs' allegations do not raise a strong

inference that Defendants acted with scienter in failing to disclose this information before this date. The more plausible and compelling inferences to be drawn from these allegations is that before February 2005, Defendants did not know that any Tysabri user had developed PML because no one knew—the symptoms were attributed to other causes—and that Defendants timely disclosed this information after they became aware of it.

Plaintiffs also allege no facts indicating that Defendants acted with scienter to conceal the PML diagnosis after this date by waiting until February 28, 2005 to disclose the two PML cases. Defendants are permitted a reasonable amount of time to evaluate potentially negative information and to consider appropriate responses before a duty to disclose arises. *See, e.g., Higginbotham v. Baxter Int'l Inc.*, 495 F.3d 753, 761 (7th Cir. 2007) ("Taking the time necessary to get things right is both proper and lawful. Managers cannot tell lies but are entitled to investigate for a reasonable time until they have a full story to reveal.").

An alternative and much more reasonable inference is that Defendants used this time to investigate, to gather more information, and to confer with Biogen and the FDA before taking any action. Consistent with this inference, defendant Martin stated that Defendants first learned of the two PML cases on February 18, 2005 and that Elan, Biogen, and the FDA made the decision to withdraw Tysabri approximately four to five days later. (¶ 323.) Likewise, James Mullen, Biogen's CEO, stated that the first case of PML was reported to the FDA on February 18, 2005, as soon as Biogen received information about it. (Aaron Decl. Ex. 12.)

### b. Defendants' knowledge regarding Tysabri and non-PML opportunistic infections

Plaintiffs allege that Defendants' knowledge of the opportunistic infections in the Tysabri clinical trials is indicated by: (1) "[D]efendants' own admissions at the March 2006 FDA Hearing"; (2) the Collaboration Agreement between Elan and Biogen, which "required Defendants to closely monitor and exhaustively review all aspects of all phases of the clinical trials"; (3) the fact that most Tysabri clinical trials were completed by early 2004; and (4) accounts of confidential sources who alleged that "Defendants knew of adverse events that were reported during Tysabri clinical trials, before the Class Period." (¶ 141.)

Plaintiffs do not allege that Defendants knew of any statistically significant or causal relationship between non-PML opportunistic infections and Tysabri during the Class Period. In fact, they do not allege that evidence of such a relationship existed during this time. Therefore, Plaintiffs fail to allege facts supporting Defendants' scienter with respect to the nondisclosure of information regarding non-PML opportunistic infections.

In *Carter-Wallace II*, the Second Circuit again considered whether Carter-Wallace had violated Section 10(b) in connection with statements regarding its epilepsy drug Felbatol. 220 F.3d at 38–39. The specific question before the court was whether plaintiffs had adequately pled scienter by alleging that Carter-Wallace had placed advertisements touting Felbatol's "unprecedented safety profile" while it was receiving reports of illness in patients taking Felbatol, including reports of aplastic anemia, the fatal bone marrow condition with which Felbatol was ultimately linked. *Id.* at 38, 40. Plaintiffs argued that Carter-Wallace had engaged in "conscious misbehavior" supporting

an inference of scienter by "recklessly, if not intentionally, perpetrating fraud by allowing the advertisements to continue when it was aware of reports that undermined the accuracy of the advertisements." *Id.* at 40. The Second Circuit rejected this argument, noting that isolated adverse event reports do not establish a causal relationship with the drug, and that it was therefore not reckless for Carter-Wallace to treat these reports as "random and statistically insignificant" until a statistically significant link was demonstrated. *Id.* at 41. The court also pointed out that "[s]ome adverse events may be expected to occur randomly, especially with a drug designed to treat people that are already ill." *Id.*

The court held that the fact that the statements at issue were made *before* a statistically significant relationship between Felbatol and any adverse event was established was "[f]atal to [the plaintiffs'] argument." *See id.* at 42. The court reaffirmed its statement from *Carter-Wallace I* that "'Carter-Wallace had no sound reason to doubt the commercial viability of Felbatol . . . until the reports of Felbatol-associated deaths became statistically significant'" *Id.* at 41 (quoting *Carter-Wallace I,* 150 F.3d at 157). Moreover, "there can be no presumption that Carter-Wallace was aware of a statistically significant connection between Felbatol and aplastic anemia" before such a connection was actually known. *Id.* at 42. The court further stated that while "the early medical reports may have indicated a potential problem, . . . until a connection between Felbatol and any illness could be made, we would not expect Carter-Wallace to abandon its product on what, at the time, would have been speculation." *Id.*

Plaintiffs' allegations regarding Defendants' "admissions" at the March 2006 FDA Hearing apparently refer to summaries of safety data presented by Dr. Panzara, a

Biogen representative, and Dr. McDermott, an FDA representative. Drs. Panzara and McDermott acknowledged that some number of non-PML opportunistic infections had occurred in Tysabri subjects during clinical trials, and that two had resulted in death. (*see* ¶¶ 142–50; *supra* note 24.) As discussed above, Defendants only concluded that there "*may* be an increased risk of other opportunistic infections." (Aaron Decl. Ex. 5 at 65 (emphasis added).) Even if this were sufficient to establish a relationship between Tysabri and non-PML opportunistic infections, Plaintiffs' allegations do not indicate when the relevant safety data were analyzed or when Defendants in fact became aware of the results.[28] *Cf. In re Biogen Idec, Inc. Sec. Litig.*, No. 05-10400-WGY, slip op. at 24 (D. Mass. Oct. 25, 2007) ("[T]he plaintiffs fail to provide even one specific factual allegation that any of the defendants learned of the allegedly adverse clinical data.").

Furthermore, a determination of whether there was a causal relationship between Tysabri and opportunistic infections was complicated by the Tysabri clinical trial subjects' use of other medications. Two of the three PML cases occurred in individuals who were concurrently receiving Avonex as part of Tysabri combination therapy trials. (Aaron Decl. Ex. 5 at 61.) The third PML case occurred in an individual with a history of chronic immunosuppressant use. (*Id.* Ex. 5 at 61.) The "black box" warning added to the Tysabri labeling upon its reintroduction to the market in July 2006 states, "Although the cases of PML were limited to patients with recent or concomitant exposure to immunomodulators or immunosuppressants, there were too few cases to rule out the

[28] Plaintiffs suggest that something less than a "strong inference" should be required where information relevant to scienter is exclusively in Defendants' knowledge and control. (Pls.' Opp'n Br. at 16–17.) However, "the PSLRA effectively shifted the burden to plaintiffs to acquire particularized knowledge of a party's *scienter* prior to obtaining discovery." *In re Bisys Sec. Litig.*, 496 F. Supp. 2d 384, 387 (S.D.N.Y. 2007).

possibility that PML may occur with Tysabri monotherapy." (*Id.* Ex. 10 at 1.) With respect to opportunistic infections generally, Dr. Panzara observed that the opportunistic infections that occurred during Tysabri treatment "were seen mostly in Crohn's disease patients with significant comorbidity or the use of immunomodulators or immunosuppressants." (*Id.* Ex. 5 at 66.) Four of the five non-PML opportunistic infections reported by Dr. Panzara occurred during Crohn's disease trials. (*Id.* Ex. 5 at 61–64.) *Cf. In re Bayer AG Sec. Litig.*, No. 03 Civ. 1546, 2004 WL 2190357, at *3 (S.D.N.Y. Sept. 30, 2004) (noting the FDA's "caveat" that a condition reported in an adverse event report "may not result from the drug but from 'the underlying disease for which the drug was given,' other medications being taken, or even 'by chance'").

With respect to the Collaboration Agreement, even if we accept Plaintiffs' contention that Elan and Biogen were required under the agreement to "closely monitor" the Tysabri clinical trials and to share information regarding adverse events (¶¶ 151–52),[29] this does not give rise to any inference that either Elan or Biogen concluded during the Class Period that an adverse event report indicated the occurrence of an opportunistic infection or that any reported opportunistic infection was causally related to Tysabri.

Plaintiffs allege that Defendants knew about Tysabri-related opportunistic infections because clinical trials were completed during the Class Period, and that "Defendants had access to, and conducted as a matter of course, an exhaustive analysis of the results in those trials." (¶ 153.) However, Plaintiffs do not allege that all Tysabri

[29] Biogen's allegation that "senior executives at Elan and Biogen, including Defendant Kelly [sic] . . . were charged with approving and closely monitoring the progress of the development and marketing of Tysabri, including the manner in which clinical trials were designed and conducted, the tracking of adverse events, the resolution of issues as they arose and communication of issues and findings to one another" is a legal conclusion regarding the interpretation of the Collaboration Agreement, and does not address whether or when a causal relationship between adverse events and Tysabri was established. (¶ 91.)

clinical trials were completed during the Class Period or that data from completed trials provided evidence of a statistically significant link between Tysabri and non-PML opportunistic infections. According to Plaintiffs' allegations, the ENCORE Phase III Crohn's disease trial, the SENTINEL Phase III MS trial and the Phase II RA trials were still ongoing as of February 28, 2005. (¶ 105.) In addition, Dr. Panzara testified at the March 2006 FDA Hearing that, with respect to adverse events, "the one thing that had changed since the time of initial approval is infection." (Aaron Decl. Ex. 5 at 49.) This suggests that the possible risk of "other opportunistic infections" described by Dr. Panzara only became apparent from later clinical trial data that were not analyzed during the Class Period.

Plaintiffs also rely on CS 4's curiously vague statement that Elan senior management was aware before November 2004 that Tysabri left patients "vulnerable" to opportunistic infections. (¶ 127.) While a generous reading of this statement suggests that Elan knew of data indicating that Tysabri increased the risk of opportunistic infection, the Court cannot credit this allegation. Plaintiffs do not allege any facts indicating that CS 4 was in a position to have knowledge regarding communications with Elan senior management or the conclusions reached by Elan senior management upon receipt of this information. *See, e.g., Novak*, 216 F.3d at 314 (holding that confidential sources must be "described in the complaint with sufficient particularity to support the probability that a person in the position occupied by the source would possess the information alleged."). As noted previously, CS 4's disclosure that he was "intimately involved" in the clinical trials is inadequate. CS 4's statement also would not establish support Defendants' knowledge of material information regarding an association between

Tysabri and non-PML opportunistic infections because it is far too vague with respect to what information was actually communicated and what conclusions any defendant actually reached. This ambiguous allegation cannot support an inference of scienter, much less a "strong inference."

Plaintiffs allege that CS 5, a neurologist who was "directly involved" with the Tysabri MS trials, stated that at least three opportunistic infections had occurred during the Tysabri MS and Crohn's disease trials and that Defendants had access to these data. Like Plaintiffs' description of CS 4, the description of CS 5 as "directly involved" in the MS trials is insufficient to support a likelihood that CS 5 would know what information was communicated to Elan executives. Furthermore, CS 5 does not assert that these opportunistic infections occurred during the Class Period or that they revealed a statistically significant association with Tysabri. Finally, it is not reasonable to infer, as Plaintiffs propose, that Defendants were "fully aware" of these infections at the time simply because they had access to the clinical trial data.

Of Plaintiffs' other confidential sources, only CS 7 asserted that Defendants knew about opportunistic infections that occurred during Tysabri clinical trials.[30] (¶ 159.) CS 7 stated that she was "certain that Defendants were aware of any concerns relating to the clinical trials." Plaintiffs' description of CS 7 does not support a likelihood that she would possess this knowledge. A data entry clerk in a clinical trial does not ordinarily

[30] CS 2 alleged that "there was a concern at Biogen that Tysabri might leave people unable to deal with other infections" and that the scientific team was generally aware of this concern. (¶ 160.) Even if this concern had been communicated to Elan (which Plaintiffs do not allege), a mere concern regarding opportunistic infections is not material information. There were publicly disseminated "concerns" about Tysabri. The need to address such concerns is, of course, one of the primary reasons why clinical trials are undertaken. The relevant issues here are (1) whether those concerns were borne out by the clinical trials, *i.e.*, did the trials yield evidence of a causal link between opportunistic infections and Tysabri, and (2) if so, when this link was established.

participate in discussions with the sponsor's executives. In addition, it is unclear from CS 7's statement what sort of "concerns" she alleges Defendants were aware of.

**c. Plaintiffs' alleged "pattern evidence"**

According to Plaintiffs, Elan restated its earnings in 1999 after an SEC review and was the subject of an SEC investigation and a shareholder lawsuit in 2002 arising from Elan's allegedly improper accounting practices. (¶ 172.) Defendants settled the shareholder lawsuit for $75 million and settled the SEC investigation by paying a civil penalty of $15 million. (¶ 173.)

Plaintiffs contend that these allegations regarding prior misconduct constitute "pattern evidence" supporting an inference of scienter. The cases cited by Plaintiffs indicate only that past misconduct of the same type as the misconduct alleged in the complaint might support an inference of scienter. *See In re Qwest Commc'n Int'l, Inc. Sec. Litig.*, 387 F. Supp. 2d 1130, 1138–39, 1147 (D. Colo. 2005) (pattern of "accounting manipulations and misrepresentations" supported inference of scienter with respect to other accounting manipulations); *Pippenger v. McQuik's Oilube, Inc.*, 854 F. Supp. 1411, 1419 (S.D. Ind. 1994) (stating that scienter may be "established by a pattern of intentional deception" though plaintiffs did not allege a pattern of deception); *In re Enron Corp. Sec., Derivative & ERISA Litig.*, 235 F. Supp. 2d 549, 689 (S.D. Tex. 2002) (stating that unspecified misconduct, though time-barred, was admissible as "evidence of a scheme and/or scienter"). Because accounting-related misconduct is not similar to the nondisclosure of adverse events, Plaintiffs' allegations regarding prior misconduct add little if anything to support an inference of scienter.

### d. Defendants' alleged failure to disclose information to the FDA

Similarly Plaintiffs argue that Defendants' "deliberate scheme" to conceal opportunistic infections from the FDA supports an inference of scienter. (Pls.' Opp'n Br. 29.)

According to Plaintiffs, the opportunistic infections that occurred during Tysabri clinical trials were "serious adverse events" or "serious adverse drug events" as defined by the FDA and were required to be documented in writing and disclosed promptly to the FDA. (¶¶ 130–35.) Plaintiffs allege that Defendants did not disclose any of the opportunistic infections that occurred during the Tysabri clinical trials until after November 2004. (¶ 136.)

Plaintiffs base their assertion on an "exhaustive search" of the FDA website, which uncovered no evidence that Defendants disclosed opportunistic infections before November 2004. (¶ 140.) In a November 23, 2004 memo from Dr. David Ross, the Deputy Director of the FDA committee that approved Tysabri, Dr. Ross stated, "[t]he events reported do not appear to represent infections due to opportunistic pathogens." (Aaron Decl. Ex. 17 at 9.) In addition, the documents outlining the scope of FDA approval do not mention opportunistic infections.[31] (¶ 140.) However, the March 2006 FDA Hearing revealed that in fact, opportunistic infections had occurred during the Tysabri clinical trials. (*See, e.g.*, ¶¶ 142–50.)

Plaintiffs' allegation that Defendants withheld information from the FDA is contradicted by the documents upon which the Complaint relies. The Center for Drug

[31] The CDER Medical Review on which the November 2004 approval of Tysabri was based did mention a report of pulmonary aspergillosis, an infeetion which was later determined to have been opportunistic. (¶ 140 n.11.) The Medical Review explicitly stated that the infection was of some concern because "a mechanistic relationship to [Tysabri] is plausible." (Aaron Decl. Ex. 4 at 55–56.)

Evaluation and Research Medical Review, which reviewed the data submitted in connection with the May 2004 BLA for Tysabri and recommended granting Tysabri accelerated approval, was based on adverse events in ongoing clinical trials that occurred on or before April 30, 2004. (Aaron Decl. Ex. 4 at 55.) Dr. Ross's memorandum is a summary of the data and analysis in the Medical Review. (*See, e.g., id.* Ex. 17 at 8; *compare* Aaron Decl. Ex. 17 at 8 *with* Aaron Decl. Ex. 4 at 54.) Therefore, Dr. Ross's comments do not refer to any adverse events that occurred after this date. By contrast, the safety data presented at the March 2006 FDA Hearing reflect data from completed studies, involving many more patients and a longer duration of exposure. (*See* Aaron Decl. Ex. 5 at 48; *compare* Aaron Decl. Ex. 4 at 54 *with* Aaron Decl. Ex. 5 at 49–50.)

Furthermore, Plaintiffs make no allegation that anyone at the FDA believes that Elan or Biogen withheld any safety information, which is especially telling in light of the fact that the FDA held a two-day hearing largely devoted to the discussion of the allegedly concealed safety data. (¶ 354; Aaron Decl. Ex. 5.)

Because Plaintiffs make no creditable allegation that any safety data were withheld from the FDA, this is not a basis for an inference of scienter.

## III. Defendants' Sarbanes-Oxley Certifications

Plaintiffs argue that the Sarbanes-Oxley Certifications accompanying Defendants' 2003 Form 20-F were false and misleading because "Defendants lacked the necessary controls to ensure that adverse events were reported to the FDA in a timely manner" and that "Defendants violated Section 13(b)(2)(B) of the [1934 Act] by misrepresenting that Elan maintained adequate internal controls, when in fact, Elan's controls were deficient,

allowing Defendants to engage in the fraud alleged herein."[32] (¶ 204.) The "disclosure controls" described in the certifications govern the treatment of information required to be disclosed in SEC filings. (*See, e.g.*, ¶ 203); 17 C.F.R. §§ 240.13a-15(e), 240.15d-15(e). The "internal control over financial reporting" described in the certification refers to processes that ensure reliable financial information and financial statements. (*See, e.g.*, ¶ 201); 17 C.F.R. § 240.15d-15(f). Section 13(b)(2)(B) of the 1934 Act requires an issuer of securities to maintain reasonable "internal accounting controls" to ensure accurate accounting and financial reporting. *See* 15 U.S.C.A. § 78m(b)(2)(B). None of these "controls" implicate the disclosure of adverse event data to the FDA, nor do Plaintiffs' allegations indicate that Defendants withheld any such information. Furthermore, because Plaintiffs do not allege that Defendants made any misstatement or omission regarding financial or accounting information, the "internal accounting controls" required under Section 13(b)(2)(B) are not implicated by Plaintiffs' Complaint.

## IV. Defendants' Ability to Detect Opportunistic Infections

Finally, Plaintiffs assert that Tysabri clinical trials did not include "the full range of medical tests necessary to timely detect symptoms of serious opportunistic infections, such as lumbar punctures, routine blood tests, and neurological examinations." Even if accepted as true, this fact would not make any of Defendants' statements misleading

[32] Plaintiffs also contend that the certifications were false and misleading because "Defendants violated [the Sarbanes-Oxley Act] . . . by issuing the false certifications." (¶ 204.) The bald assertion that the certifications were false provides no explanation why the certification was fraudulent and therefore fails to satisfy the Rule 9(b) requirement that fraud must be pled with particularity. *Rombach v. Chang*, 355 F.3d 164, 175 (2d Cir. 2004) ("To meet the pleading requirement of Rule 9(b), plaintiffs cannot rest on their say-so that these statements are fraudulent; they must explain why. Having neglected to do so, they fail to plead with the requisite particularity."). In any case, as discussed above, Plaintiffs do not adequately allege that the 2003 Annual Report or any of Defendants' statements during the Class Period contained any materially misleading statement or omission.

because Plaintiffs do not identify any representation by Defendants regarding Elan and/or Biogen's ability to detect opportunistic infections in its clinical trials or about the specific tests utilized for this purpose. As previously noted, the allegations that Defendants did not have adequate procedures to determine whether or not an infection was opportunistic merely undercuts their claim that defendants were aware of and concealed such infections.

## V. Section 20(a) Liability

Under Section 20(a), an individual can be liable for aiding and abetting a violation of the securities laws if he "controls" another individual who has committed a violation. Liability under Section 20(a) requires an underlying violation by a "controlled" person. *Boguslavsky v. Kaplan*, 159 F.3d 715, 720 (2d Cir. 1998). Because Plaintiffs do not state a claim for violation of the securities laws by any of the Defendants, they do not state a claim for liability under Section 20(a). *Id.*

## CONCLUSION

Because the Court finds that Plaintiffs have failed to adequately plead both materiality and scienter, we do not reach the remaining arguments offered by Defendants in support of their motion to dismiss. Defendants' motion to dismiss **[31]** is GRANTED and Plaintiffs' Complaint is dismissed in its entirety.

In their opposition brief, Plaintiffs requested leave to amend their Complaint in the event of dismissal. *See Van Buskirk v. New York Times Co.*, 325 F.3d 87, 91 (2d Cir. 2003) ("[I]t is often appropriate for a district court, when granting a motion to dismiss for

failure to state a claim, to give the plaintiff leave to file an amended complaint."). Plaintiffs are permitted to file a motion for leave to amend in which they set forth their proposed amendments.

SO ORDERED.

Dated: New York, New York
March 27, 2008

Richard J. Holwell
United States District Judge